REMARKS

Upon entry of the Amendment, claims 1, 2, 4, 6, 12-15, 20, and 28-37 are pending in the application. Claims 3 and 19 have been canceled. Claims 1, 2, 6, 12-15, 28, 29, 31, 32, 34, 35 and 37 have been amended. Claim 16 and 37 have been withdrawn.

I. Priority

The Examiner asserts that the certified copy of the priority document is not present in the USPTO file.

The present application comes from a PCT application. Pursuant to MPEP § 201.13(b) and PCT Rule 17.2, Applicants respectfully request that a certified copy of the priority document be retrieved from the International Bureau.

II. Claim Objections

The Examiner asserts that the claims and/or the specification are not in full compliance with 37 C.F.R. § 1.821(d).

Without admitting that the objection is correct, Applicants respectfully submit that the claims refer to appropriate sequence identifiers. Claims 1-2, 12-15, 28, 31, and 34 recite the sequence identifier SEQ ID NO: 1 or SEQ ID NO: 2.

III. Claim Rejections - 35 U.S.C. § 101

Claim 19 has been rejected under 35 U.S.C. § 101 allegedly because the claimed invention is directed to non-statutory subject matter.

Without admitting that the rejection is correct, Applicants respectfully submit that claim 19 has been canceled. Therefore, this rejection is moot.

IV. Claim Rejections - 35 U.S.C. § 112

(1) Claims 1-4, 6, 12-15, 19, 20, and 28-36 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

The Examiner contends that the claim language "PyrGlu^{32} to Val^{478}" is indefinite because:

> (a) the numbering is allegedly meaningless without reference to a particular sequence,
>
> (b) the numbers are internally inconsistent. Specifically, according to the Examiner, if PyrGlu is at position 32, then the recited valine would be at position 509, not 478, and
>
> (c) the symbol "~" to show a range of amino acids is not standard in the art.

Without admitting that the rejection is correct, claims 1, 12-15, 28, 31, 34, and 35 have been amended to recite a polypeptide having the amino acid sequence of SEQ ID NO: 1 or a polypeptide having the amino acid sequence of SEQ ID NO: 2. Further, claims 2, 6, 20, 29, 32, and 35 recite a polypeptide having the amino acid sequence of SEQ ID NO: 2. None of these claims contain the claim language "PyrGlu^{32} to Val^{478}."

Further, the Examiner contends that the claim language "deletion, substitution or addition of one or several amino acids" in claims 1, 2, 12-15, 28, 31 and 34 is indefinite.

Without admitting that the rejection is correct, claims 1, 2, 12-15, 28, 31 and 34 have been amended. Claims 1, 12-15, 28, 31 and 34 have been amended to recite a polypeptide having the amino acid sequence of SEQ ID NO: 1 or a polypeptide having the amino acid sequence of SEQ ID NO: 2. Claim 2 has been amended to recite a polypeptide having the amino acid sequence of SEQ ID NO: 2. None of these claims contain the claim language "deletion, substitution or addition of one or several amino acids."

(2) Claims 1, 2, 12-15, 28, 31 and 34 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly not being in compliance with the written description requirement.

Without admitting that the rejection is correct, claims 1, 2, 12-15, 28, 31, and 34 have been amended. Claims 1, 12-15, 28, 31 and 34 have been amended to recite a polypeptide having the amino acid sequence of SEQ ID NO: 1 or a polypeptide having the amino acid sequence of SEQ ID NO: 2. Claim 2 has been amended to recite a polypeptide having the amino acid sequence of SEQ ID NO: 2. Referring to page 6 of the Office Action, the Examiner acknowledges that SEQ ID NO: 1 and 2 meet the written description provision of 35 U.S.C. § 112, first paragraph. Given that claims 1, 12-15, 28, 31, and 34 recite SEQ ID NO: 1 and SEQ ID NO: 2 and that claim 2 recites SEQ ID NO: 1, amended claims 1, 2, 12-15, 28, and 34 meet the written description provision of 35 U.S.C. § 112, first paragraph.

Reconsideration and withdrawal of these rejections under 35 U.S.C. § 112 are respectfully requested.

V. Claim Rejections - 35 U.S.C. § 103

(1) Claims 1-4, 19, and 20 have been rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Date *et al.* ("Date") in view of EP 0461560 ("EP '560").

Claim 1 presently recites a neovascularization inhibitor composition comprising a pharmaceutically acceptable carrier with a polypeptide having the amino acid sequence of SEQ ID NO: 1 or a polypeptide having the amino acid sequence of SEQ ID NO: 2.

Further, claims 2 and 20 recite a polypeptide having the amino acid sequence of SEQ ID NO: 2.

With respect to SEQ ID NO: 1, the Examiner asserts that Date teaches HGF/NK4. The Examiner also asserts that Date necessarily teaches using HGF/NK4 in a pharmaceutically acceptable formulation.

Applicants respectfully submit that Date fails to teach or suggest the claimed neovascularization inhibitor composition. Date teaches that HGF/NK4 is an antagonist of HGF, and abrogates the mitogenic, motogenic, and morphogenic activities of HGF. Date discloses that HGF/NK4 competitively inhibited the specific binding of HGF to the receptor. *See* Abstract. Further, Date discloses that HGF/NK4 almost completely inhibited the mitogenic, motogenic, and morphogenic activities of HGF. *See* Abstract and page 3046. However, Date fails to disclose the inhibitory activity of neovascularization as provided by a polypeptide having the amino acid sequence of SEQ ID NO: 1, i.e., Date fails to teach or suggest the neovascularization inhibitor composition recited in claim 1.

EP '560 fails to provide the deficiencies of Date. EP '560 discloses a HGF having the amino acid sequence shown in Figure 2 thereof from Met^{1} to Ser^{728} and a HGF having the amino acid sequence shown in Figure 3 thereof from Met^{1} to Ser^{723}. EP '560 fails to teach a polypeptide having the amino acid sequence of SEQ ID NO: 1 or SEQ ID NO: 2. Further, EP '560 fails to teach the inhibitory activity of neovascularization. In this regard, EP '560 fails to provide the deficiencies of Date.

With respect to SEQ ID NO: 2, a person of ordinary skill in the art would not have been motivated to replace HGF/NK4 disclosed in Date with a human leukocyte-derived HGF disclosed in EP '560.

Date is deficient in that it fails to teach a polypeptide having the amino acid sequence of SEQ ID NO: 2. EP '560 is relied upon to alleviate this deficiency. Figure 3 of EP '560 discloses the amino acid sequence of a human leukocyte-derived HGF thereof.

Applicants respectfully submit that EP '560 fails to provide the deficiencies of Date. Figure 3 of EP '560 discloses an amino acid sequence different from the amino acid sequence of SEQ ID NO: 2. In this regard, each of Date and EP '560 both fail to teach or suggest the amino acid sequence of SEQ ID NO: 2.

Further, a person of ordinary skill in the art would not have been motivated to modify the HGF/NK4 disclosed in Date into a polypeptide having the amino acid sequence of SEQ ID NO: 2. In contrast to the 447 amino acids present in HGF/NK4, the amino acid sequence of SEQ ID NO: 2 provides for 442 amino acids. There is no suggestion to delete the five consecutive amino acids at positions 131 to 135 in HGF/NK4. These deleted amino acids are present in the first of four Kringle domains present at positions 95 to 176 of HGF/NK4. The amino acids at positions 131 to 135 in HGF/NK4 are -Phe-Leu-Pro-Ser-Ser-.

Furthermore, the human leukocyte derived HGF disclosed in EP '560 contains several amino acids different from SEQ ID NO: 2. A person of ordinary skill in the art would not have been motivated to make the necessary modifications so that the human leukocyte derived HGF disclosed in EP '560 would have the amino acid sequence of SEQ ID NO: 2.

Claim 4 depends from claim 1 or claim 2. In this regard, claim 4 is nonobvious for at least the same reasons as claims 1 and 2.

(2) Claims 12-15 and 28-36 have been rejected under 35 U.S.C. § 103 as allegedly being unpatentable over U.S. Patent No. 6,207,152 to Schwall *et al.* ("Schwall '152") in view of Date and EP '560.

Each of claims 12-15, 28, 31, and 34 presently recite a polypeptide having the amino acid sequence of SEQ ID NO: 1 or a polypeptide having the amino acid sequence of SEQ ID NO: 2.

Each of claims 29, 32, and 35 recite a polypeptide having the amino acid sequence of SEQ ID NO: 2.

A person of ordinary skill in the art would not have been motivated to use the protein disclosed in Date or EP '560 in a method disclosed in Schwall '152.

Schwall '152 discloses a method of treating cancer in a mammal which entails administering an effective amount of a HGF receptor agonist. Schwall is deficient in that it fails to teach a polypeptide having the amino acid sequence of SEQ ID NO: 1 or a polypeptide having the amino acid sequence of SEQ ID NO: 2.

Date and EP '560 are relied upon to alleviate this deficiency. As described above, Date discloses HGF/NK4 as an antagonist of HGF. EP '560 discloses a human leukocyte-derived HGF.

There is no motivation to select the HGF/NK4 disclosed in Date or the human leukocyte-derived HGF disclosed in EP '560. Schwall '152 fails to disclose the inhibitory activity of neovascularization. As described above, both Date and EP '560 fail to teach or suggest the inhibitory activity of neovascularization. In this regard, Date and EP '560 fail to alleviate the deficiencies of Schwall '152. Further, Schwall '152 fails to suggest using a polypeptide having

the amino acid sequence of SEQ ID NO: 1 or a polypeptide having the amino acid sequence of SEQ ID NO: 2 to treat cancer.

Further, with respect to SEQ ID NO: 2, EP '560 fails to provide the deficiencies of Date and Schwall '152. As described above, the human leukocyte-derived HGF disclosed in EP '560 is different from a polypeptide having the amino acid sequence of SEQ ID NO: 2. Further, EP '560 and Schwall '152 fail to motivate a person of ordinary skill in the art to modify the amino acid sequence of the human leukocyte-derived HGF to the amino acid sequence of SEQ ID NO: 2.

Claim 30 depends from claim 28 or claim 29. In this regard, claim 30 is nonobvious for at least the same reasons as claims 28 and 29.

Claim 33 depends from claim 31 or claim 32. In this regard, claim 30 is nonobvious for at least the same reasons as claims 31 and 32.

Claim 36 depends from claim 34 or claim 35. In this regard, claim 36 is nonobvious for at least the same reasons as claims 34 and 35.

Reconsideration and withdrawal of these rejections under 35 U.S.C. § 103 are respectfully requested.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

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